

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1-2. (canceled)

3. (currently amended) A method for determining the sensitivity of a proliferative disease in a subject to in response to a combined treatment with an mTOR inhibitor and a cytotoxic agent, comprising determining the status presence of the wild type p53 (TP53) gene, a mutated p53 (TP53) gene, or the absence, deficiency or deletion of the of p53 (TP53) gene and/or the level of expression/post-translational modification of p53 in a sample derived from the subject.

4. (previously presented) A method according to claim 3, wherein the proliferative disease comprises a cancer.

5. (canceled)

6. (previously presented) A method according to claim 3, wherein the sample is derived from a tumor in the subject.

7. (currently amended) A method of selecting subjects suffering from a proliferative disease for a combined treatment with an mTOR inhibitor and a cytotoxic agent, comprising determining the sensitivity of the proliferative disease to the combined treatment in each said subjects subject by a the method as described in claim 3, and selecting these said subjects showing wild-type p53 (TP53) status for the combined treatment.

8. (previously presented) A method according to claim 3, wherein the mTOR inhibitor comprises rapamycin or a rapamycin derivative.

9. (previously presented) A method according to claim 8, wherein the rapamycin derivative comprises 40-O-(2-hydroxyethyl) rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin or 40-epi-(tetrazolyl)-rapamycin.

10. (previously presented) A method according to claim 3, wherein the cytotoxic agent is selected from an antineoplastic antimetabolite, a platin compound, an alkylating agent, a topoisomerase I or II inhibitor, a microtubule active agent and irradiation.

11-12. (canceled)

13. (currently amended) A method for determining the sensitivity or response of a proliferative disease in a subject to a treatment with an mTOR inhibitor in combination with a cytotoxic agent, said method comprising:

- a. treating said subject with an mTOR inhibitor and a cytotoxic agent,
- b. removing a tissue sample from the subject suffering from said proliferative disease;
and
- c. determining in a sample derived from the subject the level of p21 expression in said tissue.

14. (currently amended) A method for enhancing the activity of a cytotoxic agent or for overcoming resistance to a cytotoxic agent in a subject treated with said cytotoxic agent, comprising

- determining the level of p21 expression in a sample derived from the subject,
- if p21 expression is upregulated after administration of a cytotoxic agent, administering to said subject a ~~therapeutically effective amount of~~ an mTOR inhibitor in combination with the cytotoxic agent,
- determining again the level of p21 expression in a new sample derived from the subject after the treatment with the combination of the mTOR inhibitor and the cytotoxic agent, and
- if p21 expression is downregulated, further treating the subject with the mTOR inhibitor either concomitantly or sequentially with said cytotoxic agent.